

Corneal Biomechanics as a Function of Race

THESIS

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Preethi Chidambaram

Undergraduate Program in Biomedical Engineering

The Ohio State University

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Thesis Committee:

Dr. Jun Liu

Dr. Cynthia Roberts, Advisor

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## Abstract

Corneal biomechanical properties are known to vary across age, gender, and race. This study aims to explore the differences in corneal biomechanics between different races, in vivo, using corneal deformation response to an applied air puff with the CorVis ST. This preliminary prospective study focuses on young normal subjects, ages 18-30. Thus far, 16 Caucasian subjects and 23 South Asian subjects have been enrolled, and three measurements were taken of each eye with the CorVis ST, as well as Pentacam, Ocular Response Analyzer (ORA), Goldmann Applanation Tonometer (GAT), and Pascal Dynamic Contour Tonometer (DCT). The subjects' data was compared to the other race and to an existing database of CorVis exams from Italian and Brazilian subjects, matched by biomechanically corrected IOP, central corneal thickness, and age. The stiffness parameter (SP), corneal velocity, deformation amplitude (DA) ratio, and maximum inverse radius were compared between groups. ANOVA tests were performed between groups for each of these parameters using Statistical Analysis Software (SAS). As greater stiffness is associated with greater resistance to deformation, a stiffer cornea would have a higher stiffness parameter, lower corneal velocity, smaller deformation amplitude ratio, and smaller maximum inverse radius. Significant differences ( $p \leq 0.05$ ) were found between the Caucasian subjects and the mixed-race database with regards to SP and corneal velocity, with Caucasian subjects having a greater SP and lower velocity, and therefore a stiffer cornea. South Asian subjects had significantly higher SP and significantly lower corneal velocity than the mixed-race database, showing that South Asians had stiffer corneas than the subjects in the database. Caucasian subjects had significantly lower DA ratio and maximum inverse radius than the South Asian subjects. These are the most sensitive CorVis parameters, and the results show that South Asian subjects have softer, more compliant corneas. These results are notable because

these differences in corneal biomechanics by race are evident even with a small number of subjects and in a young population. Corneal biomechanical properties affect the accuracy of IOP measurements, disease development, and response to surgery, so further exploring corneal biomechanical differences by race could be very valuable.

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## Vita

June 2013 .....Dublin Coffman High School  
2013-present.....Undergraduate, Department of Biomedical  
Engineering, The Ohio State University

## Fields of Study

Major Field: Biomedical Engineering

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## Chapter 1: Introduction

Corneal biomechanical properties affect surgical outcomes, intraocular pressure (IOP) measurements, disease diagnosis and disease progression<sup>1</sup>. Corneal biomechanical differences have been shown in diseases like Fuch's endothelial dystrophy<sup>2</sup> and keratoconus<sup>3</sup>. Because of aforementioned effect on IOP measurements, corneal biomechanical properties are especially important when discussing glaucoma and ocular hypertension. Therefore, it is critical to understand corneal biomechanical properties.

The cornea is a viscoelastic material, which means it has properties of both viscous and elastic materials and that its response to applied force is time dependent<sup>4</sup>. According to LaPlace's law, membrane stress of a shell with finite thickness is dependent on the internal fluid pressure. LaPlace's law can be used to show that biomechanical responses of the globe are dependent on the pressure inside the globe<sup>5</sup>. Therefore, IOP is a confounding factor in corneal biomechanics measurements<sup>6</sup>.

Corneal properties, specifically central corneal thickness (CCT), and corneal biomechanical parameters, specifically corneal hysteresis (CH) and corneal resistance factor (CRF) have been shown to vary across demographics, such as age, gender, and race<sup>7-19</sup>. CCT is the thickness of the cornea, and is measured by pachymetry. CCT, while not a measure of biomechanics, affects measurements of the stiffness of the cornea. A thicker cornea would lead to greater resistance to deformation, and therefore the cornea would appear stiffer<sup>20</sup>. CH and CRF are measured using the Ocular Response Analyzer, and both are affected by viscoelasticity of the cornea<sup>4</sup>. CH is the difference in applanation pressures, and is descriptive of the response differences of the cornea during the loading and unloading phases<sup>21</sup>. The equation to calculate CRF was developed empirically, which resulted in a linear combination of the applanation

pressures that produced the strongest correlation to CCT.<sup>4</sup> The same CH can occur at high or low elasticity dependent on viscosity<sup>22</sup>. Essentially, the cornea's deformation response is time-dependent<sup>23</sup> due to its viscoelastic nature. Additionally, as the subject's IOP changes, the timing of inward applanation changes, which affects the magnitude of maximum applied pressure from the ORA, meaning CH and CRF are also IOP-dependent measurements<sup>4</sup>. This makes interpretation of the produced parameters more complicated. Therefore, though differences in corneal biomechanics have been shown across demographics using the ORA, further work is warranted to define the effects of age, race, and gender on biomechanics in more detail.

This preliminary prospective study aims to measure corneal biomechanical deformation response while accounting for the confounding factors of IOP and corneal thickness. It will also consider the time-dependent response of the cornea and test corneas under the same loading conditions, and then compare deformation response parameters to explore the presence of corneal biomechanical differences between Caucasians and South Asians.

## Chapter 2: Methods

### *Subjects*

A total of 39 subjects between the ages of 18-30 were prospectively enrolled in this study, 16 Caucasian and 23 South Asian. To be included in the study, subjects had to be able to consent, self-identify as Caucasian or South Asian, have a clear cornea, and be able to undergo all testing at time of enrollment. Subjects were excluded if they were pregnant or had any eye infections, cataracts, glaucoma, or any previous ophthalmic surgeries, as these factors could impact corneal biomechanics.

Subjects were recruited by sending the recruitment flier to student groups on Ohio State's campus. Potential subjects were also referred to the study team by other subjects.

### *Measurements*

Measurements for this study were taken with the Pentacam, Ocular Response Analyzer (ORA), CorVis ST, Goldmann Applanation Tonometer (GAT), and Pascal Dynamic Contour Tonometer (DCT), shown in Figure 1. They were taken in the order in which they are listed, for ease of testing. Three measurements were taken of each eye with each instrument.



Figure 1: Devices used for testing (L-R) Pentacam, ORA, CorVis ST, GAT, Pascal DCT

The Pentacam (OCULUS, Inc.) takes a series of cross-sectional images of a patient's anterior chamber and combines them to create a three-dimensional model, which allowed for shape and volume of the anterior chamber to be found. It also reports information about the central corneal curvature.

The ORA (Reichert Technologies) is an air puff test and is used to measure corneal hysteresis (CH), corneal resistance factor (CRF), and corneal compensated intraocular pressure (IOPcc). Because corneal properties affect IOP measurements, the ORA takes these into account and produces IOPcc, a measurement of IOP that is less affected by corneal properties.

The CorVis ST (OCULUS, Inc.) uses an air puff to deform the cornea and captures a video of the deformation response of the patient's cornea. Analysis of the video collected by the CorVis allowed quantification of biomechanical deformation response parameters. The CorVis also outputs a biomechanically corrected IOP (bIOP), an empirical value that takes CCT, age, and dynamic corneal response parameters into account<sup>24</sup>.

The GAT (Haag Streit Group) is a common measure of IOP that uses a probe to touch a patient's eye to measure IOP. Before using the GAT, a numbing fluorescein drop is placed in each eye. However, this measurement is affected by central corneal thickness and corneal stiffness. The data collected from this was compared to the IOP data collected by the ORA and the Pascal DCT.

The Pascal DCT (Ziemer Ophthalmic Systems AG) is similar to the GAT in that a probe touches a patient's eye to measure IOP. A numbing fluorescein drop is also put in each eye before use of the Pascal DCT. However, the Pascal DCT is a digital tonometer that uses contour measurements to determine the IOP. Therefore, this IOP measurement is relatively unaffected by corneal properties and CCT<sup>25</sup>.

### *Comparison*

Subjects in the three groups were matched by bIOP, CCT, and age, with age having the lowest weight. All eyes that had a match were used. The stiffness parameter (SP), corneal velocity, deformation amplitude (DA) ratio, and maximum inverse radius were compared between each set of subjects. The DA ratio and maximum inverse radius have been shown to be the most sensitive CorVis parameters<sup>24</sup>. Statistical Analysis Software (SAS) was used to plot these parameters against bIOP for each race. An ANOVA test was conducted using SAS to determine whether there is a significant difference ( $p < 0.05$ ) in corneal biomechanical properties among the tested races.

### Chapter 3: Results

After matching, 28 eyes from 14 Caucasian subjects, 23 eyes from 16 South Asian subjects, and 102 eyes from 102 subjects from the mixed-race database were included.

Information on matching parameters for the Caucasian and South Asian subjects can be found in Table 1.

Table 1: Age, CCT, and IOP for Caucasian and South Asian subjects

	Age (years)	CCT ( $\mu\text{m}$ )	bIOP (mmHg)
Caucasian (n=28)	$22.2 \pm 1.10$	$556 \pm 21.6$	$14.8 \pm 2.31$
South Asian (n=23)	$20.8 \pm 2.13$	$546 \pm 24.6$	$14.5 \pm 2.27$
p-value	0.109	0.134	0.593

The average age of the subjects from the mixed-race database (n=102) was  $24.5 \pm 4.95$  years, with a p-value of 0.005 compared to Caucasians and a p-value of  $<0.001$  compared to South Asians. The average CCT of the subjects from the mixed-race database was  $551 \pm 22.2$   $\mu\text{m}$ , with a p-value of 0.430 compared to Caucasians and a p-value of 0.270 compared to South Asians. The average bIOP of the subjects from the mixed-race database was  $14.8 \pm 2.25$  mmHg, with a p-value of 0.950 compared to Caucasians and a p-value of 0.477 compared to South Asians.

The majority of results were taken from the output of the CorVis ST, which is shown in Figure 2.

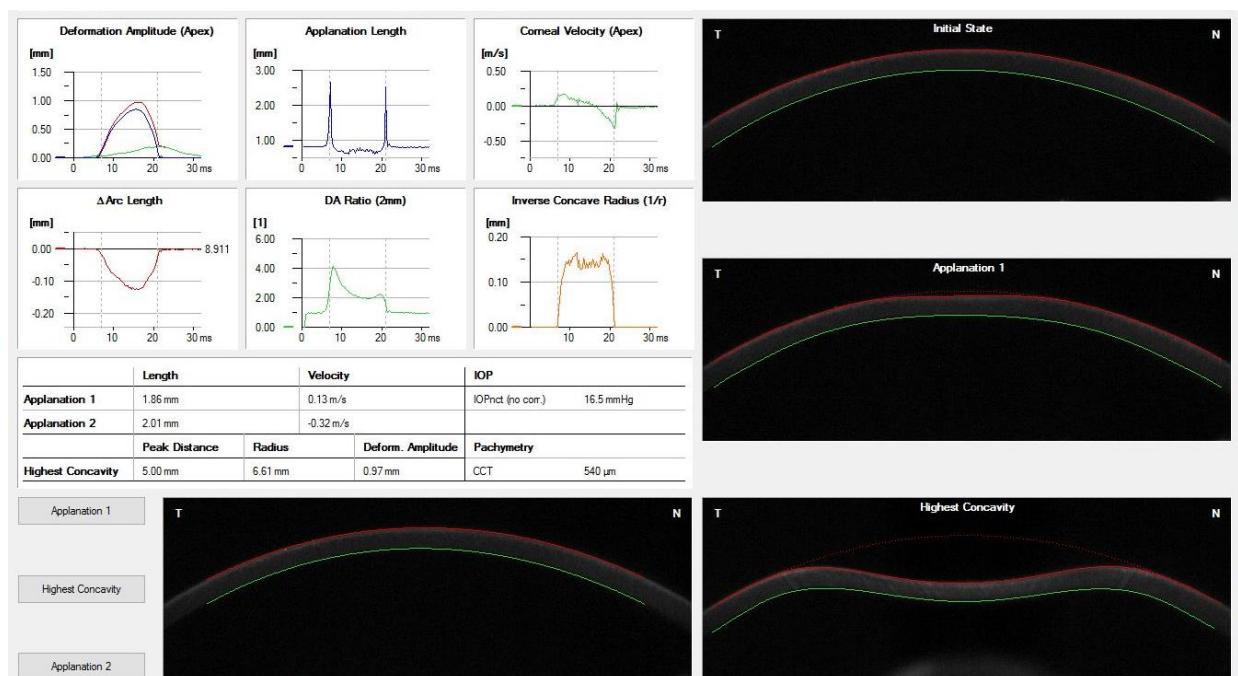


Figure 2: CorVis ST output, showing important response parameters like corneal velocity, deformation amplitude ratio, and inverse radius

After matching by bIOP, CCT, and age, the average SP, corneal velocity, DA ratio, and maximum inverse radius were found for each subject group. These parameters were plotted against the bIOP for each race group using SAS. These plots are shown in Figure 3.



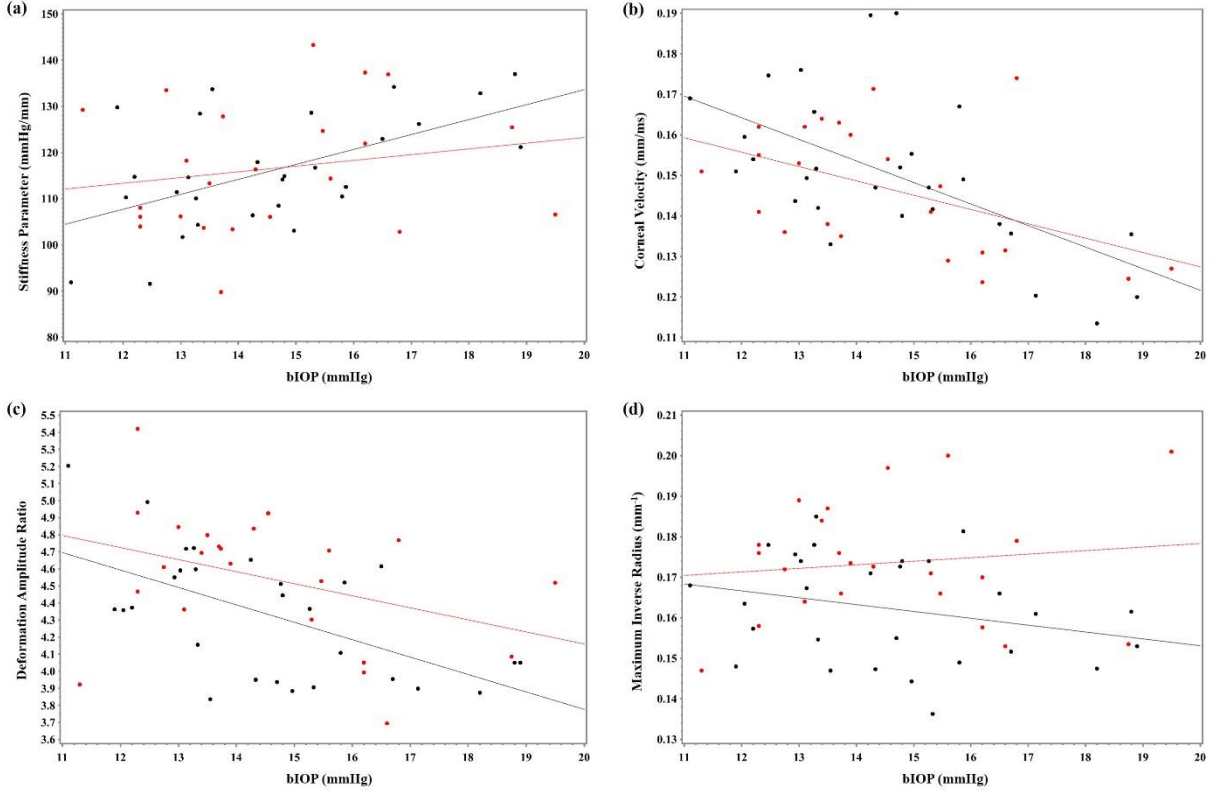


Figure 3: Plots of relevant parameters vs. bIOP for Caucasians (black) and South Asians (red), including: (a) stiffness parameter, (b) corneal velocity, (c) deformation amplitude ratio, and (d) maximum inverse radius

For Caucasians and South Asians, the relevant parameters and the corresponding p-values from the ANOVA test are shown in Table 2.

Table 2: Averages of relevant parameters for Caucasians and South Asians

	Stiffness Parameter (mmHg/mm)	Corneal Velocity (mm/ms)	Deformation Amplitude Ratio	Max. Inverse Radius ( $\text{mm}^{-1}$ )
Caucasian (n=28)	$116 \pm 12.2$	$0.150 \pm 0.019$	$4.33 \pm 0.368$	$0.162 \pm 0.013$
South Asian (n=23)	$116 \pm 13.9$	$0.147 \pm 0.016$	$4.55 \pm 0.396$	$0.174 \pm 0.015$
p-value	0.928	0.468	0.051	0.014

The average SP of the subjects from the mixed-race database (n=102) was  $106 \pm 17.1$  mmHg/mm, with a p-value of 0.004 compared to Caucasians and a p-value of 0.006 compared to

South Asians. The average corneal velocity of the subjects from the mixed-race database was  $0.161 \pm 0.018$  mm/ms, with a p-value of 0.007 compared to Caucasians and a p-value of 0.001 compared to South Asians. The average DA ratio of the subjects from the mixed-race database was  $4.39 \pm 0.398$ , with a p-value of 0.483 compared to Caucasians and a p-value of 0.082 compared to South Asians. The average maximum inverse radius of the subjects from the mixed-race database was  $0.165 \pm 0.017$  mm<sup>-1</sup>, with a p-value of 0.439 compared to Caucasians and a p-value of 0.022 compared to South Asians.

## Chapter 4: Discussion

The stiffness parameter is the applied load divided by the amount of deformation. Since a stiffer cornea would have greater resistance to deformation, it would have a smaller amount of deformation, and therefore a higher SP. A stiffer cornea would also have a smaller corneal velocity because it would have greater resistance to the applied force and therefore could not be moved at as high of a speed as a softer cornea. The deformation amplitude ratio is the ratio of the deformation of the middle of the cornea to the deformation of the points 2 mm away from the middle. A softer cornea would have more deformation in the middle, and therefore would have a higher DA ratio. The maximum inverse radius is the inverse of the radius of curvature of the cornea at highest concavity. A softer cornea would have a smaller radius of curvature, and therefore a higher maximum inverse radius<sup>26</sup>.

There were significant differences shown between Caucasian subjects and the mixed-race database with regards to the SP and corneal velocity, with Caucasian subjects having a higher SP and a lower corneal velocity. These results showed that the Caucasian subjects had a stiffer cornea. However, because the database was composed of more than one race, as well as individuals of mixed race, no definitive conclusions can be drawn.

There were also significant differences shown between South Asian subjects and the mixed-race database with regards to these same parameters, with South Asian subjects also having a higher SP and a lower corneal velocity, which would indicate a stiffer cornea. Additionally, South Asians had a significantly higher maximum inverse radius than the mixed-race database, which would indicate a softer cornea. These results contradict each other, perhaps because the database was of multiple races or because of the low number of subjects.

Caucasians and South Asians were near significance threshold, and significantly different, respectively, for the two parameters, DA ratio and maximum inverse radius, which are the two most sensitive parameters output by the CorVis ST. South Asians had a near significance threshold higher DA ratio and a significantly higher maximum inverse radius. It is expected that the difference in DA ratio would become significantly different with a larger number of subjects. These results indicate that South Asians have softer, more compliant corneas than Caucasians.

These results align with a previous study that showed that South Asians have softer corneas than Caucasians. In this study, Kondapalli et al. prospectively enrolled subjects of five different races: Asian (n=14), South Asian (n=15), Black (n=18), Hispanic (n=15), and Caucasian (n=15). One eye per subject underwent the following tests: GAT, Pascal DCT, ORA, Schiotz tonometry, axial length, keratometry, and pachymetry. There was no significant difference in IOP for the tested subjects. Significant differences were found using 5g load and 7g load Schiotz tonometry between Caucasians and all other races. There were no significant differences between any of the other races. South Asians were found to have a significantly lower Schiotz reading than Caucasians. As Schiotz tonometry is a measure of scleral rigidity, and without IOP differences between the groups, it was concluded that South Asians had less rigid corneas<sup>27</sup>. Our findings are also consistent with this conclusion.

Another study explored the differences in CCT within a large multi-ethnic population. Retrospectively reviewing charts of patients in Northern California who were above the age of 40 and had a record CCT measurement, Wang et al. found that Asians have thinner corneas than Caucasians, but thicker corneas than black subjects. Additionally, when analyzing Asian subgroups, they found that South and Southeast Asians have thinner corneas than East Asians<sup>18</sup>. As we matched by CCT, we did not find significant differences in CCT between our subjects of

different races. Our matching allowed us to look solely at the material properties of the cornea. However, as CCT does affect stiffness of the cornea<sup>20</sup>, it would be important to consider this while looking at corneal biomechanical properties.

We theorize that because of the limited number of subjects in both of our race categories, parameters other than DA ratio and maximum inverse radius may not have shown significant differences. Therefore, it is certainly worth studying more subjects of these races to explore corneal biomechanical differences via analysis of deformation response. Other limitations of this study also include the match by bIOP. With a greater number of subjects in the race categories, it might be more useful to match by Pascal IOP, which is less affected by corneal properties<sup>25</sup>. Additionally, we only looked at a limited age range, and it is important to explore how corneal biomechanics differ by race, with age differences as well. Finally, we did not match subjects by gender, which also influences biomechanical properties. With a greater number of subjects, this match would be possible as well.

## Chapter 5: Conclusions

We conclude that there are significant differences in corneal biomechanical response parameters between Caucasians and South Asians, with South Asians having softer, more compliant corneas based on the two most sensitive CorVis parameters. This noted difference by race could be used to study differences in disease progression, response to surgery, and IOP measurement between these two groups. As this difference could affect treatment planning, it would be important to explore the variations in corneal biomechanical properties between other races, as well.

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